CLAIMS

1. A monoclonal antibody that binds human notum pectinacetylesterase (NOTUM) and neutralizes at least one activity of NOTUM, wherein the antibody reduces NOTUM activity in a trisodium 8-octanoyloxypyrene-1,3,6-trisulfonate (OPTS) assay in vitro and reduces NOTUM activity in a Wnt signaling assay in vitro.

2. The antibody of claim 1, wherein the antibody binds to a NOTUM selected from mouse NOTUM, guinea pig NOTUM, cynomolgus monkey NOTUM, and rhesus monkey NOTUM.

3. The antibody of any one of the preceding claims, wherein upon administration to a subject the antibody increases serum PINP levels *in vivo*, increases bone mineral density *in vivo*, increases midshaft femur cortical thickness *in vivo*, increases midshaft femur bone area *in vivo*, increases midshaft humerus cortical thickness *in vivo*, increases endocortical bone formation *in vivo*, increases the proportion of cortical bone volume in the LV5 vertebral body *in vivo*, and/or increases the proportion of femoral neck bone volume to femoral neck total volume *in vivo*.

4. The antibody of any one of the preceding claims, wherein the antibody binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with K_D of less than 50 nM.

5. The antibody of claim 4, wherein the K_D is less than 20 nM.

6. The antibody of claim 5, wherein the K_D is less than 10 nM.

7. The antibody of any one of the preceding claims, wherein the antibody has at least one binding characteristic selected from:

a) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 83 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 84;

b) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 85 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 86;

c) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 94;

d) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 99;

e) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 95 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 2;

f) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO: 8;

g) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 15 and a light chain variable region having the amino acid sequence of SEQ ID NO: 16;

h) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 23 and a light chain variable region having the amino acid sequence of SEQ ID NO: 24;

i) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 31 and a light chain variable region having the amino acid sequence of SEQ ID NO: 32;

j) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 39 and a light chain variable region having the amino acid sequence of SEQ ID NO: 40;

k) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 47 and a light chain variable region having the amino acid sequence of SEQ ID NO: 48; and

l) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 55 and a light chain variable region having the amino acid sequence of SEQ ID NO: 56.

8. The antibody of any one of the preceding claims, wherein the antibody is selected from a mouse antibody, a chimeric antibody, a humanized antibody, and a human antibody.

9. The antibody of claim 1, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein:

a) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 9, a CDR2 having the amino acid sequence of SEQ ID NO: 10, and a CDR3 having the amino acid sequence of SEQ ID NO: 11, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 12, a CDR2 having the amino acid sequence of SEQ ID NO: 13, and a CDR3 having the amino acid sequence of SEQ ID NO: 14; or

b) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 91, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 22; or

c) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 17, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 19, and the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 20, a CDR2 having the amino acid sequence of SEQ ID NO: 21, and a CDR3 having the amino acid sequence of SEQ ID NO: 22; or

d) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 30; or

e) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 25, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 28, a CDR2 having the amino acid sequence of SEQ ID NO: 29, and a CDR3 having the amino acid sequence of SEQ ID NO: 30; or

f) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 91, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 38; or

g) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 33, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 35, and the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 36, a CDR2 having the amino acid sequence of SEQ ID NO: 37, and a CDR3 having the amino acid sequence of SEQ ID NO: 38; or

h) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 41, a CDR2 having the amino acid sequence of SEQ ID NO: 42, and a CDR3 having the

amino acid sequence of SEQ ID NO: 43, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 44, a CDR2 having the amino acid sequence of SEQ ID NO: 45, and a CDR3 having the amino acid sequence of SEQ ID NO: 46; or

i) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 49, a CDR2 having the amino acid sequence of SEQ ID NO: 50, and a CDR3 having the amino acid sequence of SEQ ID NO: 51, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 52, a CDR2 having the amino acid sequence of SEQ ID NO: 53, and a CDR3 having the amino acid sequence of SEQ ID NO: 54; or

j) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 57, a CDR2 having the amino acid sequence of SEQ ID NO: 58, and a CDR3 having the amino acid sequence of SEQ ID NO: 59, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 60, a CDR2 having the amino acid sequence of SEQ ID NO: 61, and a CDR3 having the amino acid sequence of SEQ ID NO: 62.

10. The antibody of claim 9, wherein:

a) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 7 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 8; or

b) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 15 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 16; or

c) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 71 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 73; or

d) the heavy chain comprises the amino acid sequence of SEQ ID NO: 72 and the light chain comprises the amino acid sequence of SEQ ID NO: 74; or

e) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 23 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 24; or

f) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 75 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 77; or

g) the heavy chain comprises the amino acid sequence of SEQ ID NO: 76 and the light chain comprises the amino acid sequence of SEQ ID NO: 78; or

h) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 31 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 32; or

i) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 79 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 81; or

j) the heavy chain comprises the amino acid sequence of SEQ ID NO: 80 and the light chain comprises the amino acid sequence of SEQ ID NO: 82; or

k) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 39 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 40; or

l) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 67 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 69; or

m) the heavy chain comprises the amino acid sequence of SEQ ID NO: 68 and the light chain comprises the amino acid sequence of SEQ ID NO: 70; or

n) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 47 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 48; or

o) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 55 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 56; or

p) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 63 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 65; or

q) the heavy chain comprises the amino acid sequence of SEQ ID NO: 64 and the light chain comprises the amino acid sequence of SEQ ID NO: 66.

11. A pharmaceutical composition comprising the antibody of any one of the preceding claims.

12. A nucleic acid molecule comprising a polynucleotide sequence that encodes a heavy chain or a light chain of the antibody of any one of claims 1 to 10.

13. The nucleic acid molecule of claim 12, wherein the nucleic acid molecule comprises a first polynucleotide sequence that encodes the heavy chain, and a second polynucleotide sequence that encodes the light chain.

14. The nucleic acid molecule of claim 12 or claim 13, wherein the nucleic acid molecule is a vector.

15. A host cell comprising the nucleic acid molecule of any one of claims 12 to 14.

16. The host cell of claim 15, wherein the host cell comprises a first nucleic acid molecule comprising a polynucleotide sequence that encodes a heavy chain, and a second nucleic acid molecule comprising a polynucleotide sequence that encodes a light chain.

17. The host cell of claim 15, wherein the nucleic acid molecule comprises a first polynucleotide sequence that encodes the heavy chain, and a second polynucleotide sequence that encodes the light chain.

18. A method of producing an antibody of any one of claims 1 to 10 comprising incubating the host cell of claim 16 or claim 17 under conditions sufficient to express the antibody.

19. Use of the pharmaceutical composition of claim 11 in the manufacture of a medicament for stimulating endocortical bone formation in a patient.

20. Use of the pharmaceutical composition of claim 11 in the manufacture of a medicament for treating, managing, or preventing a disease or disorder characterized by bone loss in a patient.

21. The use of claim 20, wherein the disease or disorder is osteoporosis.

22. A single unit dosage form comprising the pharmaceutical composition of claim 11.

CLAIMS

1. A monoclonal antibody that binds human notum pectinacetylesterase (NOTUM) and neutralizes at least one activity of NOTUM, wherein the antibody reduces NOTUM activity in a trisodium 8-octanoyloxypyrene-1,3,6-trisulfonate (OPTS) assay in vitro and reduces NOTUM activity in a Wnt signaling assay in vitro, wherein the antibody is not a murine IgG antibody having a V_H region as defined by the amino acid sequence DVQLVESGGGLVQPGGSRKISCAASGFTFSSYGMHWVRQAPEKGLEWVAYISSSTVTTYYADTVKGRFTISRDNANNT LFLQMTSLRSEDTAMYYCSRQNWDGGYFDVWGAGTTVTVSS, and a V_L region as defined by the amino acid sequence DIVLTQSLASLAVSLGQRATISCRASKSVSSSGYSYMHWYQQKPGQPPKLLIYLASNLESGVPARFSGSGSGTDFTLNIHP VEEEDAATYYCQHSRALPLTFGAGTKLELKR.

2. A monoclonal antibody that binds human notum pectinacetylesterase (NOTUM) and neutralizes at least one activity of NOTUM, wherein the antibody comprises a heavy chain variable region and a light chain variable region, wherein:

a) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 91, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 22; or

b) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 17, a CDR2 having the amino acid sequence of SEQ ID NO: 18, and a CDR3 having the amino acid sequence of SEQ ID NO: 19, and the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 20, a CDR2 having the amino acid sequence of SEQ ID NO: 21, and a CDR3 having the amino acid sequence of SEQ ID NO: 22; or

c) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 30; or

d) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 25, a CDR2 having the amino acid sequence of SEQ ID NO: 26, and a CDR3 having the amino acid sequence of SEQ ID NO: 27, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 28, a CDR2 having the amino acid sequence of SEQ ID NO: 29, and a CDR3 having the amino acid sequence of SEQ ID NO: 30; or

e) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 90, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 91, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 92, a CDR2 having the amino acid sequence of SEQ ID NO: 93, and a CDR3 having the amino acid sequence of SEQ ID NO: 38; or

f) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 33, a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a CDR3 having the amino acid sequence of SEQ ID NO: 35, and the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 36, a CDR2 having the amino acid sequence of SEQ ID NO: 37, and a CDR3 having the amino acid sequence of SEQ ID NO: 38; or

g) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 41, a CDR2 having the amino acid sequence of SEQ ID NO: 42, and a CDR3 having the amino acid sequence of SEQ ID NO: 43, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 44, a CDR2 having the amino acid sequence of SEQ ID NO: 45, and a CDR3 having the amino acid sequence of SEQ ID NO: 46; or

h) the heavy chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 57, a CDR2 having the amino acid sequence of SEQ ID NO: 58, and a CDR3 having the amino acid sequence of SEQ ID NO: 59, and wherein the light chain variable region comprises a CDR1 having the amino acid sequence of SEQ ID NO: 60, a CDR2 having the amino acid sequence of SEQ ID NO: 61, and a CDR3 having the amino acid sequence of SEQ ID NO: 62.

3. The antibody of any one of the preceding claims, wherein:

a) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 15 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 16; or

b) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 71 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 73; or

c) the heavy chain comprises the amino acid sequence of SEQ ID NO: 72 and the light chain comprises the amino acid sequence of SEQ ID NO: 74; or

d) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 23 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 24; or

e) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 75 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 77; or

f) the heavy chain comprises the amino acid sequence of SEQ ID NO: 76 and the light chain comprises the amino acid sequence of SEQ ID NO: 78; or

g) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 31 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 32; or

h) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 79 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 81; or

i) the heavy chain comprises the amino acid sequence of SEQ ID NO: 80 and the light chain comprises the amino acid sequence of SEQ ID NO: 82; or

j) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 39 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 40; or

k) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 67 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 69; or

l) the heavy chain comprises the amino acid sequence of SEQ ID NO: 68 and the light chain comprises the amino acid sequence of SEQ ID NO: 70; or

m) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 55 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 56; or

n) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 63 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 65; or

o) the heavy chain comprises the amino acid sequence of SEQ ID NO: 64 and the light chain comprises the amino acid sequence of SEQ ID NO: 66.

4. The antibody of claim 1 or 2, wherein the antibody binds to a NOTUM selected from mouse NOTUM, guinea pig NOTUM, cynomolgus monkey NOTUM, and rhesus monkey NOTUM.

5. The antibody of any one of the preceding claims, wherein upon administration to a subject the antibody increases serum PINP levels *in vivo*, increases bone mineral density *in vivo*, increases midshaft femur cortical thickness *in vivo*, increases midshaft femur bone area *in vivo*, increases midshaft humerus cortical thickness *in vivo*, increases endocortical bone formation *in vivo*, increases the proportion of cortical bone volume in the LV5 vertebral body *in vivo*, and/or increases the proportion of femoral neck bone volume to femoral neck total volume *in vivo*.

6. The antibody of any one of the preceding claims, wherein the antibody binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with K_D of less than 50 nM.

7. The antibody of claim 6, wherein the K_D is less than 20 nM.

8. The antibody of claim 7, wherein the K_D is less than 10 nM.

9. The antibody of any one of the preceding claims, wherein the antibody has at least one binding characteristic selected from:

a) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 83 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 84;

b) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 85 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 86;

c) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 94;

d) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 1 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 99;

e) binds to a polypeptide having the amino acid sequence of SEQ ID NO: 95 with a binding affinity that is at least 5-fold stronger than the binding affinity of the antibody for a polypeptide having the amino acid sequence of SEQ ID NO: 2;

f) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 15 and a light chain variable region having the amino acid sequence of SEQ ID NO: 16;

g) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 23 and a light chain variable region having the amino acid sequence of SEQ ID NO: 24;

h) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 31 and a light chain variable region having the amino acid sequence of SEQ ID NO: 32;

i) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 39 and a light chain variable region having the amino acid sequence of SEQ ID NO: 40; and

j) competes for binding to NOTUM with an antibody comprising a heavy chain variable region having an amino acid sequence of SEQ ID NO: 55 and a light chain variable region having the amino acid sequence of SEQ ID NO: 56.

10. The antibody of any one of the preceding claims, wherein the antibody is selected from a mouse antibody, a chimeric antibody, a humanized antibody, and a human antibody.

11. A pharmaceutical composition comprising the antibody of any one of the preceding claims.

12. A nucleic acid molecule comprising a polynucleotide sequence that encodes a heavy chain or a light chain of the antibody of any one of claims 1 to 10.

13. The nucleic acid molecule of claim 12, wherein the nucleic acid molecule comprises a first polynucleotide sequence that encodes the heavy chain, and a second polynucleotide sequence that encodes the light chain.

14. The nucleic acid molecule of claim 12 or claim 13, wherein the nucleic acid molecule is a vector.

15. A host cell comprising the nucleic acid molecule of any one of claims 12 to 14.

16. The host cell of claim 15, wherein the host cell comprises a first nucleic acid molecule comprising a polynucleotide sequence that encodes a heavy chain, and a second nucleic acid molecule comprising a polynucleotide sequence that encodes a light chain.

17. The host cell of claim 15, wherein the nucleic acid molecule comprises a first polynucleotide sequence that encodes the heavy chain, and a second polynucleotide sequence that encodes the light chain.

18. A method of producing an antibody of any one of claims 1 to 10 comprising incubating the host cell of claim 16 or claim 17 under conditions sufficient to express the antibody.

19. Use of the pharmaceutical composition of claim 11 in the manufacture of a medicament for stimulating endocortical bone formation in a patient.

20. Use of a monoclonal antibody that binds human notum pectinacetylesterase (NOTUM) in the manufacture of a medicament for stimulating endocortical bone formation in a patient, wherein the antibody reduces NOTUM activity in a trisodium 8-octanoyloxypyrene-1,3,6-trisulfonate (OPTS) assay in vitro and reduces NOTUM activity in a Wnt signaling assay.

21. Use of the pharmaceutical composition of claim 11 in the manufacture of a medicament for treating, managing, or preventing a disease or disorder characterized by bone loss in a patient.

22. Use of a monoclonal antibody that binds human notum pectinacetylesterase (NOTUM) in the manufacture of a medicament for treating, managing, or preventing a disease or disorder characterized by bone loss in a patient, wherein the antibody reduces NOTUM activity in a trisodium 8-octanoyloxypyrene-1,3,6-trisulfonate (OPTS) assay in vitro and reduces NOTUM activity in a Wnt signaling assay.

23. The use of claim 21 or claim 22, wherein the disease or disorder is osteoporosis.

24. A single unit dosage form comprising the pharmaceutical composition of claim 11.